

**AMENDMENTS TO THE CLAIMS**

1. (Previously presented) A method of inhibiting a viral infection in a subject, the method comprising administering to said subject a pharmaceutical composition comprising a ceramide-generating retinoid or a pharmaceutically acceptable salt thereof.

2. (Withdrawn) A method of preventing or inhibiting a viral infection in a subject, the method comprising administering to said subject a pharmaceutical composition comprising a ceramide-degradation inhibitor or a pharmaceutically acceptable salt thereof.

3. (Withdrawn) A method of preventing or inhibiting a viral infection in a subject, the method comprising administering to said subject a pharmaceutical composition comprising:

- (a) a ceramide-generating retinoid or a pharmaceutically acceptable salt thereof; and
- (b) a ceramide-degradation inhibitor or a pharmaceutically acceptable salt thereof.

4. (Original) A method of claim 1 wherein the ceramide-generating retinoid is a retinoic acid derivative.

5. (Withdrawn) A method of claim 1 wherein the ceramide degradation inhibitor is selected from the group consisting of glucosyl ceramide synthase inhibitors, sphingosine-1-phosphate synthesis inhibitors, protein kinase C inhibitors, and the pharmaceutically acceptable salts thereof.

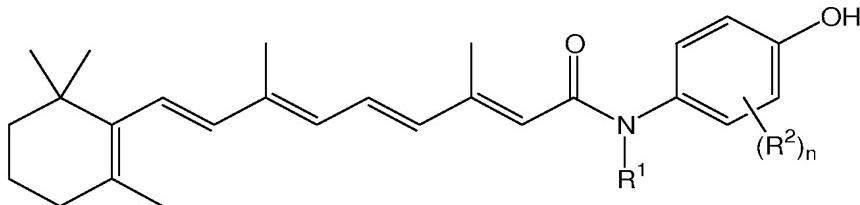
6. (Previously presented) A method of inhibiting a viral infection, the method comprising administering a pharmaceutical composition comprising at least one N-(aryl)retinamide compounds to the subject suffering from or susceptible to a viral infection.

7. (Original) The method of claim 6, wherein the N-(aryl)retinamide modulates ceramide metabolism.

Amendment Accompanying RCE dated 5/5/2011  
Response to Advisory Action of March 16, 2011

8. (Original) The method of claim 6, wherein the pharmaceutical composition comprises N-(4-hydroxyphenyl)retinamide or a derivative thereof.

9. (Original) The method of claim 6, wherein the pharmaceutical composition comprises at least one compound of the formula:



wherein:

R<sup>1</sup> is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, or optionally substituted aralkyl;

R<sup>2</sup> is independently selected at each occurrence from the group consisting of hydrogen, halogen, hydroxy, optionally substituted alkoxy, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted amino, and optionally substituted mono- and di-alkylamino; and

n is an integer of from 0 to about 4.

10. (Original) The method of claim 6, wherein the pharmaceutical composition comprises N-(4-hydroxyphenyl)retinamide.

11. (Original) The method of claim 9, wherein the pharmaceutical composition further comprises one or more therapeutic agents selected from 1-phenyl-2-hexadecanoylamino-3-morpholino-1-propanol, chemokine inhibitors, HIV fusion inhibitors, viral protease inhibitors, reverse transcriptase inhibitors, and entry inhibitors.

12. (Original) The method of claim 6, wherein the subject is a mammal.

13. (Original) The method of claim 6, wherein the subject is a primate.

14. (Original) The method of claim 6, wherein the subject is a human.

15. (Original) The method of claim 6, wherein the N-(aryl)retinamide compound inhibits HIV infectivity at a concentration of less than 10  $\mu$ M.

16. (Original) The method of claim 6, wherein the N-(aryl)retinamide compound inhibits HIV infectivity at a concentration of less than 5 $\mu$ M.

17. (Original) A method of inhibiting HIV infectivity in a subject, the method comprising administration of N-(4-hydroxyphenyl)retinamide or a derivative thereof sufficient to increase ceramide levels in a cellular membrane susceptible to HIV entry.

18. (Original) The method of claim 17, wherein the N-(4-hydroxyphenyl)retinamide or a derivative thereof decreases the viral load in a subject by about 40%.

19. (Withdrawn) A method of inhibiting HIV infectivity in a subject, the method comprising administration of compound that stimulates the *de novo* synthesis of ceramide sufficient to increase ceramide levels in a cellular membrane susceptible to HIV entry.

20. (Withdrawn) The method of claim 19, wherein the compound that stimulates the generation of ceramide is sphingomyelinase.

21. (Withdrawn) The method of claim 19, wherein sphingomyelinase decreases viral load in a subject by about 40%, at least about 50%, 60%, 75%, 80%, 99.9%, up to about 100%.

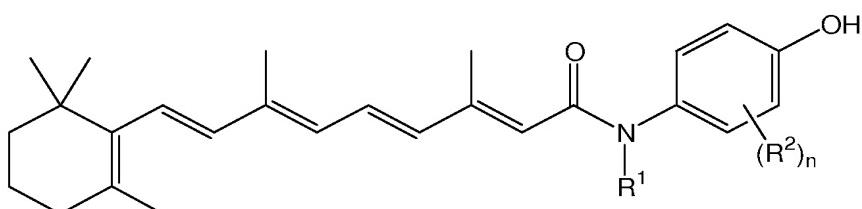
22. (Withdrawn) The method of claim 21, wherein viral load is due to infection by HIV.

23. (Currently amended) A method of inhibiting a viral attachment/entry or exit phase of a virus by administering a pharmaceutical composition to a cell susceptible to infection by a virus, wherein the pharmaceutical composition comprises an inhibitor of at least one

enzyme essential to ceramide metabolism, thereby inhibiting viral attachment/entry or exit phase of the virus.

24. (Original) The method of claim 23, wherein the enzyme is essential to a glycosylation step of ceramide metabolism.

25. (Original) The method of claim 23, wherein the pharmaceutical composition comprises at least one compound of the formula:



wherein:

$R^1$  is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, or optionally substituted aralkyl;

$R^2$  is independently selected at each occurrence from the group consisting of hydrogen, halogen, hydroxy, optionally substituted alkoxy, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted amino, and optionally substituted mono- and di-alkylamino; and

$n$  is an integer of from 0 to about 4.

26. (Original) The method of claim 25, wherein the pharmaceutical composition comprises N-(4-hydroxyphenyl)retinamide.

27. (Original) The method of claim 26, wherein the pharmaceutical composition further comprises one or more therapeutic agents selected from 1-phenyl-2-hexadecanoylamino-3-morpholino-1-propanol, chemokine inhibitors, HIV fusion inhibitors, viral protease inhibitors, reverse transcriptase inhibitors, and entry inhibitors.

28. (Original) The method of claim 25, wherein the cell is a mammalian cell.

29. (Original) The method of claim 28, wherein the cell is an immune cell.

30. (Previously presented) The method of claim 25, wherein the virus is HIV.

31. (Original) The method of claim 25, wherein the N-(aryl)retinamide compound inhibits HIV infectivity at a concentration of less than 10  $\mu$ M.

32. (Original) The method of claim 25, wherein the N-(aryl)retinamide compound inhibits HIV infectivity at a concentration of less than 5 $\mu$ M.

33. (Previously presented) The method of claim 25, wherein the at least one enzyme essential to ceramide metabolism is sphingomyelinase and the inhibitor inhibits the viral attachment/entry phase of the virus in a cell by about 40% up to about 100%.

34. (Withdrawn) A kit comprising:

- a) one or more agents for increasing ceramide concentration of a cell,
- b) means for detecting at least one of a) ceramide concentration of the cells, and 2) inhibition of viral infectivity of the cell; and
- c) directions for using the kit.

35. (Withdrawn) The kit of claim 34, wherein the agents comprise a pharmaceutical composition of a N-aryl retinamide compound capable of activating ceramide biosynthesis in addition to a pharmaceutical composition that inhibits ceramide glycosylation and (glyco)sphingolipid formation.

36. (Withdrawn) The kit of claim 34, wherein the agents comprise any one or more of compositions as identified by Formula I and substituted groups thereof.

37. (New) The method of claim 28, wherein the cell is a differentiated macrophage.